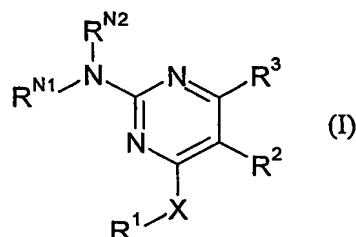


## CLAIMS

1. The use of a compound of formula I:



or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor, wherein:

X is O or NH;

R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of H, and optionally substituted C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, and phenyl-C<sub>1-4</sub> alkyl; R<sup>1</sup> is an optionally substituted C<sub>9-14</sub> aryl group or an optionally substituted C<sub>5-7</sub> aryl group;

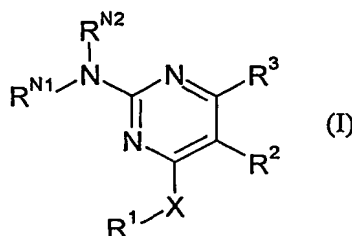
R<sup>N1</sup> and R<sup>N2</sup> are either:

- (i) independently selected from H, R, R', SO<sub>2</sub>R, C(=O)R, (CH<sub>2</sub>)<sub>n</sub>NR<sup>N3</sup>R<sup>N4</sup>, where n is from 1 to 4 and R<sup>N3</sup> and R<sup>N4</sup> are independently selected from H and R, where R is optionally substituted C<sub>1-4</sub> alkyl, and R' is optionally substituted phenyl-C<sub>1-4</sub> alkyl, or
- (ii) together with the nitrogen atom to which they are attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group.

2. The use according to claim 1, wherein R<sup>N1</sup> and R<sup>N2</sup> are independently selected from H and R.

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3. The use according to claim 2, wherein  $R^{N1}$  and  $R^{N2}$  are both H.
4. The use according to any one of claims 1 to 3, wherein  $R^2$  is H.
5. The use according to any one of claims 1 to 4, wherein  $R^3$  is methyl.
6. The use according to any one of claims 1 to 5, wherein X is NH.
7. The use according to any one of claims 1 to 6, wherein  $R^1$  is selected from an optionally substituted  $C_{9-14}$  aryl group and an optionally substituted bi- $C_{5-7}$  aryl group.
8. The use according to claim 7, wherein  $R^1$  is an optionally substituted naphthyl group.
9. The use according to claim 7, wherein  $R^1$  is an optionally substituted biphenyl group.
10. The use according to any one of claims 1 to 9, wherein the condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor is a disorder of the GI tract.
11. The use of a compound of formula I:



or a pharmaceutically acceptable salt thereof in a method of therapy, wherein:

X is O or NH;

R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of H, and optionally substituted C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, and phenyl-C<sub>1-4</sub> alkyl;

R<sup>1</sup> is an optionally substituted C<sub>9-14</sub> aryl group or an optionally substituted C<sub>5-7</sub> aryl group;

R<sup>N1</sup> and R<sup>N2</sup> are either:

(i) independently selected from H, R, R', SO<sub>2</sub>R, C(=O)R, (CH<sub>2</sub>)<sub>n</sub>NR<sup>N3</sup>R<sup>N4</sup>, where n is from 1 to 4 and R<sup>N3</sup> and R<sup>N4</sup> are independently selected from H and R, where R is optionally substituted C<sub>1-4</sub> alkyl, and R' is optionally substituted phenyl-C<sub>1-4</sub> alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group;

with the proviso that when R<sup>N1</sup>, R<sup>N2</sup> and R<sup>2</sup> are H, R<sup>3</sup> is methyl, and X is NH, then R<sup>1</sup> is not: phenyl; 3-I-phenyl, 4-Me-phenyl; 3,5-diacetyl-phenyl, 3-acetyl-phenyl; 4-acetyl-phenyl; and 2-carboxy-phenyl.

12. The use according to claim 11, wherein R<sup>N1</sup> and R<sup>N2</sup> are independently selected from H and R.

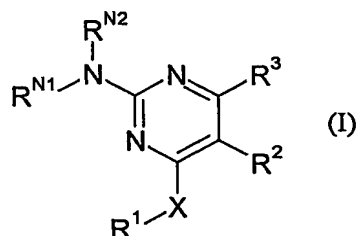
13. The use according to claim 12, wherein R<sup>N1</sup> and R<sup>N2</sup> are both H.

14. The use according to any one of claims 11 to 13, wherein R<sup>2</sup> is H.

15. The use according to any one of claims 11 to 14, wherein R<sup>3</sup> is methyl.

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16. The use according to any one of claims 11 to 15, wherein X is NH.
17. The use according to any one of claims 11 to 16, wherein R<sup>1</sup> is selected from an optionally substituted C<sub>9-14</sub> aryl group and an optionally substituted bi-C<sub>5-7</sub> aryl group.
18. The use according to claim 17, wherein R<sup>1</sup> is an optionally substituted naphthyl group.
19. The use according to claim 17, wherein R<sup>1</sup> is an optionally substituted biphenyl group.
20. A pharmaceutical composition comprising a compound of formula I as defined in any one of claims 11 to 19, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.
21. A compound of formula I:



or a salt, solvate and chemically protected form thereof, wherein:

X is O or NH;

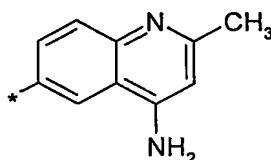
R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of H, and optionally substituted C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, and phenyl-C<sub>1-4</sub> alkyl; R<sup>1</sup> is an optionally substituted C<sub>9-14</sub> aryl group or an optionally substituted bi-C<sub>5-7</sub> aryl group;

$R^{N1}$  and  $R^{N2}$  are either:

(i) independently selected from H, R,  $R'$ ,  $SO_2R$ ,  $C(=O)R$ ,  $(CH_2)_nNR^{N3}R^{N4}$ , where n is from 1 to 4 and  $R^{N3}$  and  $R^{N4}$  are independently selected from H and R, where R is optionally substituted  $C_{1-4}$  alkyl, and  $R'$  is optionally substituted phenyl- $C_{1-4}$  alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted  $C_{5-7}$  heterocyclic group;

with the provisos that when  $R^{N1}$ ,  $R^{N2}$  and  $R^2$  are H,  $R^3$  is methyl, and X is NH, then  $R^1$  is not:



and that when  $R^{N1}$ ,  $R^{N2}$  and  $R^2$  are H,  $R^3$  is methyl, and X is NH, then  $R^1$  is not: phenyl; 3-I-phenyl, 4-Me-phenyl; 3,5-diacetyl-phenyl, 3-acetyl-phenyl; 4-acetyl-phenyl; and 2-carboxy-phenyl.

22. The compound according to claim 21, wherein  $R^{N1}$  and  $R^{N2}$  are independently selected from H and R.

23. The compound according to claim 22, wherein  $R^{N1}$  and  $R^{N2}$  are both H.

24. The compound according to any one of claims 21 to 23, wherein  $R^2$  is H.

25. The compound according to any one of claims 21 to 24, wherein  $R^3$  is methyl.

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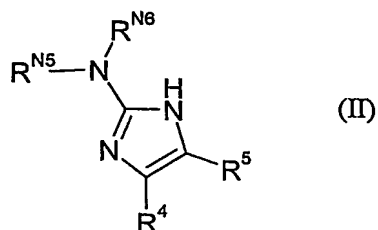
26. The compound according to any one of claims 21 to 25, wherein X is NH.

27. The compound according to any one of claims 21 to 26, wherein R<sup>1</sup> is an optionally substituted naphthyl group.

28. The compound according to any one of claims 21 to 26, wherein R<sup>1</sup> is an optionally substituted biphenyl group.

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29. The use of a compound of formula II:



or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor, wherein:

R<sup>5</sup> is selected from the group consisting of H, and optionally substituted C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, and phenyl-C<sub>1-4</sub> alkyl;

R<sup>4</sup> is an optionally substituted C<sub>9-14</sub> aryl group or an optionally substituted bi-C<sub>5-7</sub> aryl group;

R<sup>N5</sup> and R<sup>N6</sup> are either:

(i) independently selected from H, R, R', SO<sub>2</sub>R, C(=O)R, (CH<sub>2</sub>)<sub>n</sub>NR<sup>N7</sup>R<sup>N8</sup>, where n is from 1 to 4 and R<sup>N7</sup> and R<sup>N8</sup> are independently selected from H and R, where R is optionally substituted C<sub>1-4</sub> alkyl, and R' is optionally substituted phenyl-C<sub>1-4</sub> alkyl, or

(ii) together with the nitrogen atom to which they are

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attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group.

30. The use according to claim 29, wherein R<sup>N5</sup> and R<sup>N6</sup> are independently selected from H, R and C(=O)R, where R is an optionally substituted C<sub>1-4</sub> alkyl group.

31. The use according to claim 30, wherein at least one of R<sup>N5</sup> and R<sup>N6</sup> is H, and the other is selected from H and C(=O)Me.

32. The use according to any one of claims 29 to 31, wherein R<sup>5</sup> is H.

33. The use according to any one of claims 29 to 32, wherein R<sup>4</sup> is preferably a C<sub>9-14</sub> aryl group or a 3- or 4-C<sub>5-6</sub> aryl-C<sub>5-6</sub> aryl group.

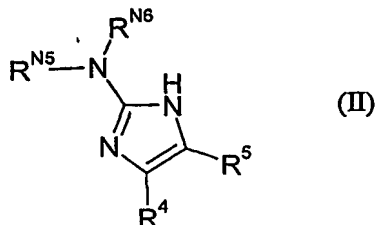
34. The use according to claim 33, wherein R<sup>4</sup> is an optionally substituted C<sub>9-14</sub> carboaryl group.

35. The use according to claim 34, wherein R<sup>4</sup> is an optionally substituted naphthyl group.

36. The use according to any one of claims 29 to 35, wherein the condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor is a disorder of the GI tract.

37. The use of a compound of formula II:

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or a pharmaceutically acceptable salt thereof, in a method of therapy, wherein:

$R^5$  is selected from the group consisting of H, and optionally substituted  $C_{1-6}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, and phenyl- $C_{1-4}$  alkyl;

$R^4$  is an optionally substituted  $C_{9-14}$  aryl group or an optionally substituted bi- $C_{5-7}$  aryl group;

$R^{N5}$  and  $R^{N6}$  are either:

(i) independently selected from H, R,  $R'$ ,  $SO_2R$ ,  $C(=O)R$ ,  $(CH_2)_nNR^{N7}R^{N8}$ , where n is from 1 to 4 and  $R^{N7}$  and  $R^{N8}$  are independently selected from H and R, where R is optionally substituted  $C_{1-4}$  alkyl, and  $R'$  is optionally substituted phenyl- $C_{1-4}$  alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted  $C_{5-7}$  heterocyclic group;

with the proviso that when  $R^{N5}$ ,  $R^{N6}$  and  $R^5$  are H,  $R^4$  is not unsubstituted 1- or 2-naphthyl or unsubstituted 4-phenyl-phenyl.

38. The use according to claim 37, wherein  $R^{N5}$  and  $R^{N6}$  are independently selected from H, R and  $C(=O)R$ , where R is preferably an optionally substituted  $C_{1-4}$  alkyl group.

39. The use according to claim 38, wherein at least one of  $R^{N5}$  and  $R^{N6}$  is H, and the other is selected from H and  $C(=O)Me$ .



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40. The use according to any one of claims 37 to 39, wherein  $R^5$  is H.

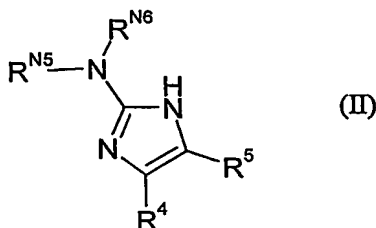
41. The use according to any one of claims 37 to 40, wherein  $R^4$  is preferably an optionally substituted  $C_{9-14}$  aryl group or an optionally substituted 3- or 4- $C_{5-6}$  aryl- $C_{5-6}$  aryl group.

42. The use according to claim 41, wherein  $R^4$  is an optionally substituted  $C_{9-14}$  carboaryl group.

43. The use according to claim 42, wherein  $R^4$  is an optionally substituted naphthyl group.

44. A pharmaceutical composition comprising a compound of formula II as defined in any one of claims 37 to 43, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

45. A compound of formula II:



or a salt, solvate and chemically protected form thereof, wherein:

$R^5$  is selected from the group consisting of H, and optionally substituted  $C_{1-6}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, and phenyl- $C_{1-4}$  alkyl;

$R^4$  is an optionally substituted  $C_{9-14}$  aryl group or an optionally substituted bi- $C_{5-7}$  aryl group;

$R^{N5}$  and  $R^{N6}$  are either:

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(i) independently selected from H, R, R', SO<sub>2</sub>R, C(=O)R, (CH<sub>2</sub>)<sub>n</sub>NR<sup>N7</sup>R<sup>N8</sup>, where n is from 1 to 4 and R<sup>N7</sup> and R<sup>N8</sup> are independently selected from H and R, where R is optionally substituted C<sub>1-4</sub> alkyl, and R' is optionally substituted phenyl-C<sub>1-4</sub> alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group;

with the provisos that when R<sup>N5</sup>, R<sup>N6</sup> and R<sup>5</sup> are H, R<sup>4</sup> is not unsubstituted 1- or 2-naphthyl or unsubstituted 4-phenyl-phenyl

and that when R<sup>N6</sup> and R<sup>5</sup> are H, and R<sup>N5</sup> is acetyl then R<sup>4</sup> is not unsubstituted 2-naphthyl.

46. The compound according to claim 45, wherein R<sup>N5</sup> and R<sup>N6</sup> are independently selected from H, R and C(=O)R, where R is preferably an optionally substituted C<sub>1-4</sub> alkyl group.

47. The compound according to claim 46, wherein at least one of R<sup>N5</sup> and R<sup>N6</sup> is H, and the other is selected from H and C(=O)Me.

48. The compound according to any one of claims 45 to 47, wherein R<sup>5</sup> is H.

49. The compound according to any one of claims 45 to 48, wherein R<sup>4</sup> is preferably an optionally substituted C<sub>9-14</sub> aryl group or an optionally substituted 3- or 4-C<sub>5-6</sub> aryl-C<sub>5-6</sub> aryl group.

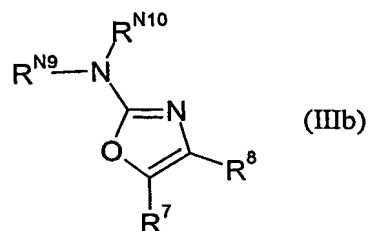
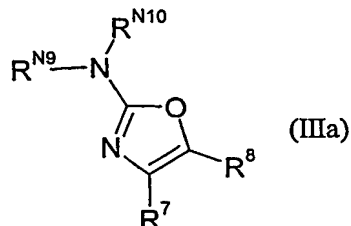
50. The compound according to claim 49, wherein R<sup>4</sup> is an optionally substituted C<sub>9-14</sub> carboaryl group.

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51. The compound according to claim 50, wherein  $R^4$  is an optionally substituted naphthyl group.

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52. The use of a compound of formula IIIa or IIIb:



or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor, wherein:

$R^8$  is selected from the group consisting of H, and optionally substituted C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, and phenyl-C<sub>1-4</sub> alkyl;

$R^7$  is an optionally substituted bi-C<sub>5-7</sub> aryl group;

$R^{N9}$  and  $R^{N10}$  are either:

(i) independently selected from H, R, R', SO<sub>2</sub>R, C(=O)R, (CH<sub>2</sub>)<sub>n</sub>NR<sup>N11</sup>R<sup>N12</sup>, where n is from 1 to 4 and R<sup>N11</sup> and R<sup>N12</sup> are independently selected from H and R, where R is optionally substituted C<sub>1-4</sub> alkyl, and R' is optionally substituted phenyl-C<sub>1-4</sub> alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group.

53. The use according to claim 52, wherein the compound is of formula (IIIb).

54. The use according to either claim 52 or claim 53, wherein  $R^8$  is selected from H and optionally substituted

C<sub>1-6</sub> alkyl.

55. The use according to claim 54, wherein R<sup>8</sup> is H or methyl.

56. The use according to any one of claims 52 to 55, wherein R<sup>N9</sup> and R<sup>N10</sup> are independently selected from H and R.

57. The use according to claim 56, wherein R is an optionally substituted C<sub>1-4</sub> alkyl group.

58. The use according to any one of claims 52 to 57, wherein R<sup>7</sup> is an optionally substituted bi-C<sub>6</sub> aryl group.

59. The use according to claim 58, wherein R<sup>7</sup> is an optionally substituted bi-phenyl group.

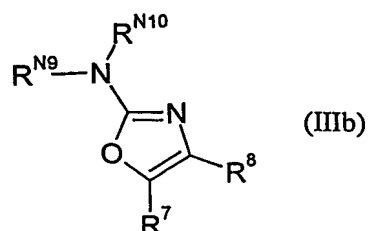
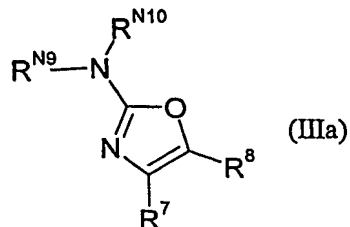
60. The use according to any one of claims 52 to 59, wherein the condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor is a disorder of the GI tract.

61. The use of a compound of formula IIIa or IIIb as defined in any one of claims 52 to 60, or a pharmaceutically acceptable salt thereof, in a method of therapy.

62. A pharmaceutical composition comprising a compound of formula IIIa or IIIb as defined in any one of claims 52 to 60, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

63. A compound of formula IIIa or IIIb:

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or a salt, solvate and chemically protected form thereof, wherein:

$R^8$  is selected from the group consisting of H, and optionally substituted  $C_{1-6}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, and phenyl- $C_{1-4}$  alkyl;

$R^7$  is an optionally substituted bi- $C_{5-7}$  aryl group;

$R^{N9}$  and  $R^{N10}$  are either:

(i) independently selected from H, R,  $R'$ ,  $SO_2R$ ,  $C(=O)R$ ,  $(CH_2)_nNR^{N11}R^{N12}$ , where n is from 1 to 4 and  $R^{N11}$  and  $R^{N12}$  are independently selected from H and R, where R is optionally substituted  $C_{1-4}$  alkyl, and  $R'$  is optionally substituted phenyl- $C_{1-4}$  alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted  $C_{5-7}$  heterocyclic group;

with the proviso that in formula IIIb, when  $R^{N9}$ ,  $R^{N10}$  and  $R^8$  are H,  $R^7$  is not 4-phenyl-phenyl.

64. The compound according to claim 63, wherein the compound is of formula (IIIb).

65. The compound according to either claim 63 or claim 64, wherein  $R^8$  is selected from H and optionally substituted  $C_{1-6}$  alkyl.

66. The compound according to claim 65, wherein  $R^8$  is H or methyl.

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67. The compound according to any one of claims 63 to 66, wherein  $R^{N9}$  and  $R^{N10}$  are independently selected from H and R.

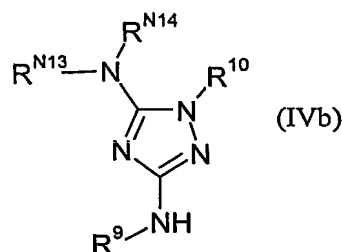
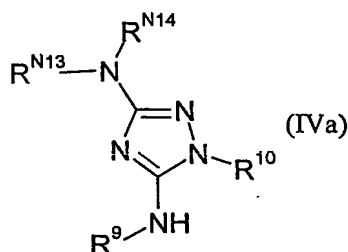
68. The compound according to claim 67, wherein R is an optionally substituted  $C_{1-4}$  alkyl group.

69. The compound according to any one of claims 63 to 68, wherein  $R^7$  is an optionally substituted bi- $C_6$  aryl group.

70. The compound according to claim 69, wherein  $R^7$  is an optionally substituted bi-phenyl group.

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71. A compound of formula IVa or IVb:



or a salt, solvate and chemically protected form thereof, wherein:

$R^{10}$  is selected from the group consisting of H and optionally substituted  $C_{1-6}$  alkyl;

$R^9$  is an optionally substituted  $C_{9-14}$  aryl group or an optionally substituted bi- $C_{5-7}$  aryl group;

$R^{N13}$  and  $R^{N14}$  are either:

- (i) independently selected from H, R,  $R'$ ,  $SO_2R$ ,  $C(=O)R$ ,  $(CH_2)_nNR^{N15}R^{N16}$ , where n is from 1 to 4 and  $R^{N15}$  and  $R^{N16}$  are independently selected from H and R, where R is optionally substituted  $C_{1-4}$  alkyl, and  $R'$  is optionally substituted phenyl- $C_{1-4}$  alkyl, or
- (ii) together with the nitrogen atom to which they are

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attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group,  
with the proviso that when R<sup>10</sup>, R<sup>N13</sup> and R<sup>N14</sup> are H, R<sup>9</sup> is not an unsubstituted naphthyl group.

72. A compound according to claim 71, wherein the compound is of formula (IVb).

73. The compound according to either claim 71 or claim 72, wherein R<sup>10</sup> is selected from H and optionally substituted C<sub>1-6</sub> alkyl.

74. The compound according to claim 73, wherein R<sup>10</sup> is methyl.

75. The compound according to any one of claims 71 to 74, wherein R<sup>N13</sup> and R<sup>N14</sup> are independently selected from H and R.

76. The compound according to claim 75, wherein R is preferably an optionally substituted C<sub>1-4</sub> alkyl group.

77. The compound according to any one of claims 71 to 76, wherein R<sup>9</sup> is an optionally substituted bi-C<sub>6</sub> aryl group.

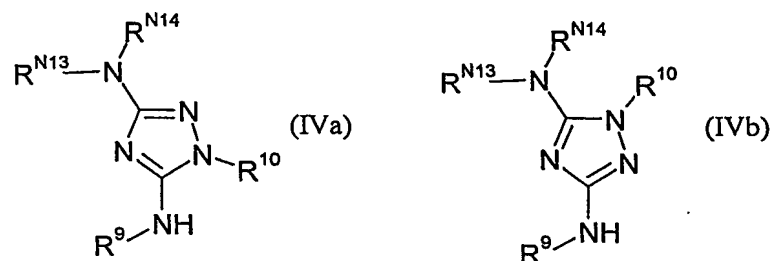
78. The compound according to any one of claims 71 to 77, wherein R<sup>9</sup> is an optionally substituted bi-phenyl group.

79. The use of a compound of formula IVa or IVb as defined in any one of claims 71 to 78, or a pharmaceutically acceptable salt thereof in a method of therapy.

80. A pharmaceutical composition comprising a compound of formula IVa or IVb as defined in any one of claims 71 to 78,

or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

81. The use of a compound of formula IVa or IVb:



or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT<sub>2B</sub> receptor, wherein:

R<sup>10</sup> is selected from the group consisting of H and optionally substituted C<sub>1-6</sub> alkyl;

R<sup>9</sup> is an optionally substituted C<sub>9-14</sub> aryl group or an optionally substituted bi-C<sub>5-7</sub> aryl group;

R<sup>N13</sup> and R<sup>N14</sup> are either:

(i) independently selected from H, R, R', SO<sub>2</sub>R, C(=O)R, (CH<sub>2</sub>)<sub>n</sub>NR<sup>N15</sup>R<sup>N16</sup>, where n is from 1 to 4 and R<sup>N15</sup> and R<sup>N16</sup> are independently selected from H and R, where R is optionally substituted C<sub>1-4</sub> alkyl, and R' is optionally substituted phenyl-C<sub>1-4</sub> alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C<sub>5-7</sub> heterocyclic group.

82. The use according to claim 81, wherein the condition which can be alleviated by antagonism of a 5-HT<sub>2B</sub> receptor is a disorder of the GI tract.

83. The use according to either claim 81 or claim 82, wherein the compound is of formula (IVb).



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84. The use according to any one of claims 81 to 83, wherein  $R^{10}$  is selected from H and optionally substituted  $C_{1-6}$  alkyl.

85. The use according to claim 84, wherein  $R^{10}$  is methyl.

86. The use according to any one of claims 81 to 85, wherein  $R^{N13}$  and  $R^{N14}$  are independently selected from H and R.

87. The use according to claim 86, wherein R is preferably an optionally substituted  $C_{1-4}$  alkyl group.

88. The use according to any one of claims 81 to 87, wherein  $R^9$  is an optionally substituted bi- $C_6$  aryl group.

89. The use according to any one of claims 81 to 88, wherein  $R^9$  is an optionally substituted bi-phenyl group.